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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/479,997	06/07/1995	DEAN ENGELHARDT	ENZ-5(D6)(C2	8799
28170	7590	11/26/2003	EXAMINER	
ENZO DIAGNOSTICS, INC. C/O ENZO BIOCHEM INC. 527 MADISON AVENUE 9TH FLOOR NEW YORK, NY 10022			MARSCHEL, ARDIN H	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	08/479,997	ENGELHARDT ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Ardin Marschel	1631	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) ~~was~~ *mailed on 5/16/03*
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 November 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____    | 6) <input type="checkbox"/> Other: _____                                    |

Continuation of Disposition of Claims: Claims pending in the application are 576,578-596,598-617,619-637,639-658,660-677,679-697,699-716,718-736,738-755,757-775,777-794 and 796-825.

Continuation of Disposition of Claims: Claims rejected are 576,578-596,598-617,619-637,639-658,660-677,679-697,699-716,718-736,738-755,757-775,777-794 and 796-825.

### **DETAILED ACTION**

The art unit designated for this application has changed. Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1631.

It is noted that a Notice of Withdrawal from Issue was mailed on May 16, 2003. Upon reconsideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

### **DRAWING OBJECTIONS**

Applicants are hereby notified that the required timing for the correction of drawings has changed. See the last 6 lines on the sheet which is attached entitled "Attachment for PTO-948 (Rev. 03/01 or earlier)". It is noted that a PTO Form 948 is mailed herewith. Due to the above notification, Applicants are required to submit drawing corrections within the time period set for responding to this Office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

### **VAGUENESS AND INDEFINITENESS**

Claims 576, 578-596, 598-617, 619-637, 639-658, 660-677, 679-697, 699-716, 718-736, 738-755, 757-775, 777-794, and 796-825 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 595 depends from claim 576 which is comprised of an oligo- or deoxyribonucleotide further comprising at least one Sig modified nucleotide. Claim 595 is vague and indefinite as to what is meant by requiring that said oligo- or polynucleotide comprises at least one ribonucleotide. Since the only two components cited in claim

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576 are either an oligo- or polynucleotide and one or more Sig modified nucleotide, it is unclear whether the ribonucleotide cited in claim 595 is a further comprising component of the claimed polymer or whether this is meant to limit the one or more Sig modified nucleotide(s). Thus the antecedent basis for the ribonucleotide limitation in claim 595 is unclear. It is noted that claim 595 does not cite the at least one ribonucleotide as "further comprising" regarding the claimed polymer content. Clarification via clearer claim wording is requested. This unclarity is also present equivalently in instant claims 615, 676, 695, 754, and 773.

All of the independent claims cite the phrase "analogs thereof" regarding BASE moieties therein. Consideration of the instant disclosure as filed as failed to reveal any definition of the metes and bounds of what is meant thereby. What constitutes an analog of a nucleobase vs. a moiety which is not an analog. Do analogs participate in hydrogen bonding or not? Is steric hindrance a defining feature regarding whether hybridization must be available for such analogs in duplex formation or not? Clarification via clearer claim wording is requested. This issue also applies to claims which depend directly or indirectly from the independent claims due to their dependence.

#### **SCOPE OF ENABLEMENT REJECTION**

Claims 576, 578-595, 617, 619-636, 658, 660-676, 697, 699-715, 736, 738-754, 775, and 777-793 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleotide containing embodiments wherein the sugar is a furanose moiety, such as ribose or deoxyribose, does not reasonably provide

enablement for any generic sugar, such as cited in claims 576 etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

Upon reconsideration of the instantly claimed sugar (SM) structures revealed that only furanose sugar moieties are disclosed which form the SM structure in oligonucleotides or polynucleotides for which attachment and/or hybridization ability are reasonably enabled. It is also noted that the early biochemical textbook of Lehninger summarized the structure of nucleic acids such as DNA on pages 638-639 as a specific structure. It is noteworthy that even though this textbook is over 30 years old the only notable backbone structure analog to be significantly utilized in biochemical reactions in

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that of peptide nucleic acids. These peptide nucleic acids, however, lack any sugar in the backbone, but rather utilize peptide bonds with spacing linkages and thus is not a nucleotide polymer. In summary, the broad "sugar" wording for the SM moiety in the instant claims does not predictably support hybridization assay practice beyond the more limited form being "furanose".

### **PRIOR ART**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 617, 619-633, 635, 637, 639-653, 655, 657, 697, 699-712, 714, 716, 718-731, 733, and 735 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Dunn et al. [Cell 12:23 (1977)].

Instant claim 617 is directed to an oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof which is construed to indicate that normal base pairing is a characteristic of the claimed oligo- or polynucleotide as is well known for nucleic acid polymers mediated by nucleobase

complementarity bonding practice. The oligo- or polynucleotide is also described in instant claim 617 as comprising at least one nucleotide modified via a covalently attached Sig moiety which is covalently attached directly or indirectly (with a chemical linkage) to a PM (phosphate moiety) therein. The Sig moiety is generic except that it must comprise a non-polypeptide, non-radioactive label. Therefore a detectable oligo- or polynucleotide which is covalently attached to a probe oligo- or polynucleotide which is complementary to a nucleic acid of interest is reasonably deemed to anticipate the above claimed subject matter. Dunn et al. at page 24 in Figure 1 depicts an adenovirus RNA/SV40 RNA conjugate wherein the SV40 RNA label is non-polypeptide and non-radioactive and attached via a phosphate to the terminal adenovirus RNA oligonucleotide which is complementary to the immobilized Ad2 DNA. This oligo- or polynucleotide thus anticipates the above listed instant claims. It is noted that instant claims such claim 621 etc. limit the chemical linkage option from claim 617 but still are deemed to include the direct phosphate linkage as in the reference and therefore are included as rejected claims herein. Instant claim 627 is included as rejected over Dunn et al. because the Sig SV40 RNA is chromogenic as being well known to be detectable via UV light.

Claims 617, 619-633, 635, 637, 639-653, 655, 657, 697, 699-712, 714, 716, 718-731, 733, and 735 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Hartmann et al. [Biopolymers 20:2635 (1981)].

The invention is as summarized above. Hartman et al. disclose in the title and abstract the formation of azoRNA for hybridization detection of genes. The Sig label is



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a yellow chromogenic label which modifies the terminal poly(A) nucleotide as required in the instant claims thus similarly anticipating the instant claims as the above Dunn et al. reference.

Claims 576, 578-593, 596, 598-613, 616, 617, 619-637, 639-658, 660-674, 677, 679-693, 696, 697, 699-716, and 718-735 are rejected under 35 U.S.C. 102(b) and (e)(2) as being clearly anticipated by Hung et al. (P/N 4,224,408).

Consideration of the above listed instant claims reveals that a non-polypeptide, non-radioactive Sig moiety covalently attached to a terminal nucleotide in an oligo- or polynucleotide or polydeoxyribonucleotide describes a generic DNA polymer. Such a DNA polymer may be envisioned as two segments. The first DNA polymer segment as the oligo- or polynucleotide or polydeoxyribonucleotide is complementary to a specific target nucleic acid via whatever nucleobase sequence is present therein. It is noted that the instant claims are not limited as to any particular sequence of desired target nucleic acid for complementarity in said first DNA polymer segment. The second and remaining DNA segment is covalently attached and thus modifies an terminal nucleotide of the first DNA segment and also is a Sig moiety as being non-polypeptide, non-radioactive and is detectable via its well known UV detectability of its nucleobase content. Thus, the above listed instant claims read on any DNA polymer. Similarly, claims which include either DNA or RNA oligo- or polynucleotides also read on any RNA polymer. The Hung et al. reference discloses both RNA and DNA, as cDNA, polymers in the abstract and throughout its disclosure as part of the synthesis disclosure therein and therefore anticipates both the instant RNA and DNA type claims as listed above. It

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is also noted that claims such as instant claims 580-582 etc. do not limit or exclude the basic DNA or RNA polymer embodiments but only limit certain additional options for instant claim embodiments and thus are also rejected hereinunder.

No claim is allowed.

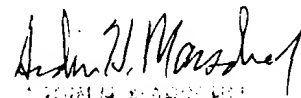
Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

November 21, 2003

  
ARDIN H. MARSCHEL  
Examiner